

# **RESPONSE**

## **DETAILED ACTION**

### ***Acknowledgements***

The Applicant gratefully acknowledges the guidance provided by the Examiner and the Examiner's Supervisor during a phone interview on 10/29/2007. The present response is based both on the Examiner action dated 10/12/2007 and the above-mentioned phone interview.

### ***Elections / Restrictions***

This response is entered without traverse, and the Examiner action to make it Final is accepted by the Applicant.

### ***Status of Claims***

To comply with Examiner action and suggestions the claims have been entered as follows. The details are further entered in the sections that follow.

Claim 1 and 2 are Currently Amended.  
Claims 3 to 5 are Canceled.  
Claim 6 is Currently Amended.  
Claims 7 to 9 are Canceled  
Claims 10 and 11 are Currently Amended.  
Claims 12 to 22 are Canceled.  
Claims 23 to 24 are Previously Presented.  
Claims 25 to 32 are Currently Amended.  
Claims 33 to 34 are Previously Presented.  
Claims 35 to 36 are Currently Amended.  
Claim 37 is Canceled.  
Claim 38 is Currently Amended.  
Claim 39 is Previously Presented.

### ***Specification***

1. The contents of the Specification have been corrected in accordance to Examiner suggestions and requirement.

Figures 1-3 and 5-7 have all been corrected. The Replacement drawings are all in concordance to originally submitted matter.

The matter of stereochemistry of [Para 59] of specification filed August 29,2007 has been corrected. The said paragraph has been replaced by the [para 75] of original specification.

[Para 107] has been replaced by [para 113] of the original submission.

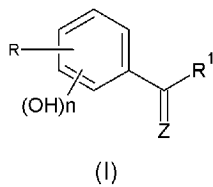
2. The informalities related to certain abbreviations not spelled out have all been deleted from the text, as said portions of the text were considered not pertinent to main discussion.
3. Substitute Specification with markings is submitted herewith. All portions deleted from the original submission are crossed out, and the replacement matter has been underlined. A clean version without markings is also supplied herewith.

### ***Claim Objections***

4. Claim 25 has been corrected in view of Examiner comment and requirement. Claim 25 (Currently Amended) reflects the changes requested by the Examiner. Additionally, claims 1, 2, and 10 have now been corrected to include their respective chemical structures and substituent limitations. These corrections are further explained below.

Please note that all chemical structures included in this Response are taken from the drawings submitted with the original submission to meet the Examiner requirements. In the claims amendments noted below, all items canceled from the previous submission are crossed out, and any new material added has been underlined.

Claim 1. (Currently Amended). A Matrix Metalloprotease, MMP, Inhibitor ~~comprising~~ consisting of at least one hydroxyaryl compound that contains an alkyl carbon side chain with a ketone group attached at the first carbon atom of the alkyl side chain, and said ketone group is directly attached to the aromatic ring at a position adjacent to hydroxyl group of hydroxyaryl ring, the chemical structure of which is in accordance to ~~Figure 4~~ formula (I):



Wherein:

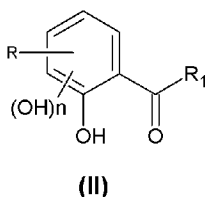
Z is O ;

(OH)<sub>n</sub> is one, two, or three OH substituents, one of which is 2-hydroxy;

R is one, two, or three substituents each independently selected from the group consisting of Alkyl, Cycloalkyl, Aryl, Cl, Br, NH<sub>2</sub>, NH-Alkyl, N(Alkyl)<sub>2</sub>, O-Alkyl, and S-Alkyl; and

R<sub>1</sub> is selected from the group consisting of Methyl, Ethyl, Alkyl, and Aryl.

Claim 2. (Currently Amended). An MMP inhibitor according to claim 1, wherein hydroxyaryl compound is selected from the group consisting of hydroxy acetophenones, ~~or~~ and hydroxy propiophenones, the chemical structure of which is in accordance to ~~Figure 2~~ formula (II):



Wherein:

(OH)<sub>n</sub> is one or two OH substituents;

R<sub>1</sub> is Methyl or Ethyl;

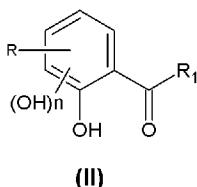
R is one, two, or three substituents each independently selected from the group consisting of Alkyl, Cycloalkyl, Aryl, Cl, Br, NH<sub>2</sub>, NH-Alkyl, N(Alkyl)<sub>2</sub>, O-Alkyl, and S-Alkyl.

Claim 10. (Currently Amended). An MMP inhibitor according to claim 1, wherein hydroxy acetophenone compound is selected from the group consisting of 2-hydroxyacetophenone, 3-hydroxyacetophenone, 4-hydroxyacetophenone, 2,3-dihydroxyacetophenone, ~~2,4-dihydroxyacetophenone~~, 2,5-dihydroxyacetophenone, 2,6-dihydroxyacetophenone, 3,4-dihydroxyacetophenone, 3,5-dihydroxyacetophenone, 2,4,6-trihydroxyacetophenone, 2,3,4-trihydroxyacetophenone, 2,3,5-trihydroxyacetophenone, 2,3,6-trihydroxyacetophenone, 2,4,5-trihydroxyacetophenone, 3,4,5-trihydroxyacetophenone, Resacetophenone, 2-Acetyl resorcinol, 4-Acetyl resorcinol, 3,4-Dihydroxyacetophenone, acetyl quinol, Quinacetophenone, 1-(3-Hydroxy-4-methoxy-5-methylphenyl) ethanone, 1-(3-hydroxy-4-methoxyphenyl) ethanone, Paeonol, Phloridzin, 5'-Bromo-2'-hydroxyacetophenone, 5'-Chloro-2'-hydroxyacetophenone, 3',5'-Dichloro-2'-hydroxyacetophenone, 3',5'-Dibromo-4'-hydroxyacetophenone, and 5-Chloro-3-bromo-2-hydroxyacetophenone, ~~or combinations thereof~~, the chemical structure of which is in accordance to ~~Figure 1~~.

5. Claims 2, 10, 27, and 28 have been corrected to reflect correct Markush language. The Applicant has also corrected claim 38

accordingly, although the Examiner did not require this correction. These corrections are further explained below.

Claim 2. (Currently Amended). An MMP inhibitor according to claim 1, wherein hydroxyaryl compound is selected from the group consisting of hydroxy acetophenones, ~~or~~ and hydroxy propiophenones, the chemical structure of which is in accordance to ~~Figure 2~~ formula (II):



Wherein:

(OH)<sub>n</sub> is one or two OH substituents;

R<sub>1</sub> is Methyl or Ethyl;

R is one, two, or three substituents each independently selected from the group consisting of Alkyl, Cycloalkyl, Aryl, Cl, Br, NH<sub>2</sub>, NH-Alkyl, N(Alkyl)<sub>2</sub>, O-Alkyl, and S-Alkyl.

Claim 10. (Currently Amended). An MMP inhibitor according to claim 1, wherein hydroxy acetophenone compound is selected from the group consisting of 2-hydroxyacetophenone, 3-hydroxyacetophenone, 4-hydroxyacetophenone, 2,3-dihydroxyacetophenone, ~~2,4-dihydroxyacetophenone~~, 2,5-dihydroxyacetophenone, 2,6-dihydroxyacetophenone, 3,4-dihydroxyacetophenone, 3,5-dihydroxyacetophenone, 2,4,6-trihydroxyacetophenone, 2,3,4-trihydroxyacetophenone, 2,3,5-trihydroxyacetophenone, 2,3,6-trihydroxyacetophenone, 2,4,5-trihydroxyacetophenone, 3,4,5-trihydroxyacetophenone, Resacetophenone, 2-Acetyl resorcinol, 4-Acetyl resorcinol, 3,4-Dihydroxyacetophenone, acetyl quinol, Quinacetophenone, 1-(3-Hydroxy-4-methoxy-5-methylphenyl) ethanone, 1-(3-hydroxy-4-methoxyphenyl) ethanone, Paeonol, Phloridzin, 5'-Bromo-2'-hydroxyacetophenone, 5'-Chloro-2'-hydroxyacetophenone, 3',5'-Dichloro-2'-hydroxyacetophenone, 3',5'-Dibromo-4'-hydroxyacetophenone, and 5-Chloro-3-bromo-2-hydroxyacetophenone, ~~or combinations thereof~~, the chemical structure of which is in accordance to Figure 4.

Claim 27. (Currently Amended). An MMP inhibitor according to claim 23, wherein a carrier base is selected from the group consisting of water and oil emulsions, suspensions, colloids, microemulsions, clear solutions, suspensions of nanoparticles, emulsions of nanoparticles, powders, ~~or~~ and anhydrous compositions.

Claim 28. (Currently Amended). An MMP inhibitor according to claim 24, wherein divalent metal ion is selected from the group consisting of copper, zinc, iron, selenium, vanadium, and manganese, ~~and combinations thereof~~.

Claim 38. (Currently Amended). An MMP inhibitor according to claim 33, wherein a carrier base is selected from the group consisting of water and oil emulsions, suspensions, colloids, microemulsions, clear solutions, suspensions of nanoparticles, emulsions of nanoparticles, powders, ~~or~~ and anhydrous compositions.

### ***Claim Rejections – 35 USC § 112***

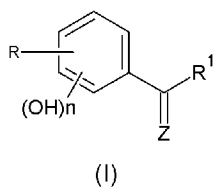
6. The Applicant acknowledges the quotation.
7. Claim 10 has been corrected to delete 2,4-dihydroxy acetophenone. The Applicant made an error in the original submission.

### ***Claim Rejections – 35 USC § 102***

8. The Applicant has corrected the language of claim 1 as per noted below:

Claim 1. **(Previously Presented)**. A Matrix Metalloprotease, MMP, Inhibitor comprising of at least one hydroxyaryl compound that contains an alkyl carbon side chain with a ketone group attached at the first carbon atom of the alkyl side chain, and said ketone group is directly attached to the aromatic ring at a position adjacent to hydroxyl group of hydroxyaryl ring, the chemical structure of which is in accordance to Figure 1.

Claim 1. **(Currently Amended)**. A Matrix Metalloprotease, MMP, Inhibitor ~~comprising~~ consisting of at least one hydroxyaryl compound that contains an alkyl carbon side chain with a ketone group attached at the first carbon atom of the alkyl side chain, and said ketone group is directly attached to the aromatic ring at a position adjacent to hydroxyl group of hydroxyaryl ring, the chemical structure of which is in accordance to ~~Figure 1~~ formula (I):



Wherein:

Z is O ;

(OH)<sub>n</sub> is one, two, or three OH substituents, one of which is 2-hydroxy;

R is one, two, or three substituents each independently selected from the group consisting of Alkyl, Cycloalkyl, Aryl, Cl, Br, NH<sub>2</sub>, NH-Alkyl,

N(Alkyl)<sub>2</sub>, O-Alkyl, and S-Alkyl; and

R<sub>1</sub> is selected from the group consisting of Methyl, Ethyl, Alkyl, and Aryl.

### ***Claim Rejections – 35 USC § 103***

9. Möller et al. (WO 03/030845 A1, published April 17, 2003) does not relate to the subject matter of the present invention. Möller et al. describes **a combination of** aromatic or heteroaromatic aldehydes and/or ketones **with a second compound**, for example, 4-Aminopyrazoline-5-one, which are useful as coloring agents, for example for hair. The present invention claims, for example, hydroxy aromatic or heteroaromatic ketones for MMP inhibition. Furthermore, hydroxy aromatic or heteroaromatic ketones are used alone, and not in combination with any other agents.

Claim 1 has now been corrected, as per the Applicant action under Item 8 above. This change of wording in claim 1 (to delete “comprising of”, and replace it with “consisting of” suggested by the Examiner) is now complied with by the Applicant.

### ***Response to Arguments***

10. The Applicant reiterates that Moller et al. teachings **must include** two components: an aromatic or heteroaromatic aldehyde or ketone, and a second component – an amine. The Examiner is suggesting that the said two ingredients **can** be present, which means that these ingredients can also perform the same function **if used alone**. That appears not to be the case, as mentioned above, that two chemical species are required concurrently.

Irrespective of the above argument, the language of the instant claims that included the word “comprising” has now been replaced by the word “consisting”, as per the Examiner suggestion made during a phone interview. It is hoped that the Examiner will find this action satisfactory.

### ***Double Patenting***

11. The Applicant makes no intention of double patenting.
12. The matter of nonstatutory obviousness-type double patenting of claims 1, 2, 10, 23, 25, and 27 over claims 1, 5, 13, and 18 of copending application 10/908,816 was discussed with the Examiner and Examiner's supervisor over a phone interview on 10/29/07. The Applicant asked the Examiner if the refiling of application 10/908,816 as a "method of skin treatment", or refiling after the removal of sections related to Resacetophenone class of ubiquitin-inhibitor agents, would circumvent the Examiner objection. The Examiner asked the Applicant to wait for Examiner's opinion on that matter. The Applicant shall resubmit application 10/908,816 after said discussion with the Examiner in due course, and at Examiner convenience.

### ***Conclusion***

It is hoped that the Examiner will kindly consider the actions in this Response and allow claims.



Shyam K Gupta  
Applicant  
5 November 2007

Attachments: the following documents are attached herewith:

1. Specification (Clean Copy)
2. Specification (Marked Copy)
3. Claims (Clean Copy)
4. Claims (Marked Copy)
5. Drawings (Replacement Sheets).